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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/749,601	12/28/2000	Nicholas C. Nicolaides	01107.00069	4817

22907 7590 06/08/2004

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EXAMINER

KRUSE, DAVID H

ART UNIT	PAPER NUMBER
	1638

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)
	09/749,601	NICOLAIDES ET AL.
	Examiner	Art Unit
	David H Kruse	1638

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

THE REPLY FILED 18 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) The period for reply expires 6 months from the mailing date of the final rejection.
 b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. The proposed amendment(s) will not be entered because:
 - (a) they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) they raise the issue of new matter (see Note below);
 - (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. Applicant's reply has overcome the following rejection(s): _____.
4. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
have been
7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: 16,17,32,33,46,56,84 and 85.

Claim(s) rejected: 1,2,5,18-20,34,35,47,77,79 and 83.

Claim(s) withdrawn from consideration: _____.

8. The drawing correction filed on _____ is a) approved or b) disapproved by the Examiner.
9. Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. Other: _____.

Continuation of 5. does NOT place the application in condition for allowance because: Applicant argues that a satisfactory disclosure of a representative number of species exists where the skilled artisan would recognize the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed (page 6, 2nd paragraph of the Remarks). This argument is not found to be persuasive because Applicant fails to adequately describe the genus of truncation mutations of a mammalian PMS2 mismatch repair gene that produce a dominant negative allele as broadly claimed. Applicant argues that the written description requirement does not require a demonstration that all dominant negative alleles of mammalian PMS2 proteins encompassed by the claims cause hypermutability in plant cells, rather, the written description requirement can be fulfilled by a disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure (paragraph spanning pages 6-7 of the Remarks). Applicant argues that the mammalian PMS2 nucleotide sequences exhibit strong homology, as demonstrate by the BLAST sequence alignment between the human and mouse PMS2 sequences already of record and that this evidences the strong conservation of PMS2 genes among widely disparate mammalian species by which the ordinarily skilled artisan would readily recognize the identity of the members of the genus of mammalian PMS2 genes (page 7, 2nd paragraph of the Remarks). This argument is not persuasive because the issue is the genus of truncation mutations that produce a dominant negative allele. Applicants argue that they have demonstrated that dominant negative alleles of human and plant PMS2 mismatch repair genes having a truncation mutation exert a dominant negative effect upon expression in plant cells to yield a hypermutable phenotype (page 7, 3rd paragraph of the Remarks). This argument is not found to be persuasive because the truncation mutations described in Figure 7, for example are of sufficient similarity in length, where as the claim is directed to any truncation mutation. Applicant argues that the specification teaches that PMS2 homologs from widely disparate species, including *Arabidopsis thaliana* and human, share a high degree of homology (page 9, 2nd paragraph of the Remarks). This argument is not found to be persuasive because the specification describes only a 31% identity, which one of skill in the art would not consider high (see Figure 2). Applicant argues that the specification teaches methods for isolating PMS2 mismatch repair genes in plant species by screening *Arabidopsis thaliana* RNA with degenerate primers derived by aligning *E. coli*, yeast, mouse, and human PMS2 genes followed by screening of an *A. thaliana* cDNA library with plant-specific primers (page 9, 4th paragraph of the Remarks). This argument is not found to be persuasive for the reasons given supra. Applicant argues that the specification teaches identification of dominant negative alleles of the plant PMS2 gene bearing a truncation mutation by analyzing the ability of the truncation mutant to generate hypermutability in a test system such as bacterial or mammalian cells (page 9, 5th paragraph of the Remarks). This argument is not found to be persuasive because a method of screening does not necessarily obviate the issue of undue trial and error experimentation. Applicant's argument as directed to Chang et al 2001 and Pang et al 1997 on pages 10-11 of the Remarks have been addressed in the Final rejection..



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